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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,906	08/16/2001	Mitchell C. Tarczynski	35718/236392 (5718-113)	1627
826	7590	02/26/2004	EXAMINER	
ALSTON & BIRD LLP BANK OF AMERICA PLAZA 101 SOUTH TRYON STREET, SUITE 4000 CHARLOTTE, NC 28280-4000			KALLIS, RUSSELL	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/930,906

Applicant(s)

TARCZYNSKI ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 3, 21-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 4-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/3/2001.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, Claims 1-2 and 4-20, and Applicant's election by telephone of SEQ ID NO: 1 in Paper No. 12/03/2003 is acknowledged.

Claims 1-26 are pending. Claims 3 and 21-26 are withdrawn. Claims 1-2 and 4-20 are examined.

Claim Objections

Claims 1, 2 and 14 are objected to because of the following informalities: The claims contain non-elected subject matter. Non-elected subject matter should be deleted from the claim.

Claim 4 is objected to because of the following informalities: The limitations recited in both sections (i) and (j) improperly refer to themselves (i.e. sections (i) and (j)).

Claim 16 is objected to because of the following informalities: The claim is drawn to specific polynucleotide sequences using GenBank Accession numbers, incorporation of essential subject material by reference is improper. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

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was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to an isolated nucleotide sequence comprising at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; a nucleotide sequence encoding an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; nucleotide sequence encoding an NADP dependent malic enzyme; and methods of increasing protein or oil production in a plant transformed therewith.

Applicant's describes the isolated polynucleotide of SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2.

Applicant does not describe any polynucleotide sequences that have at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; that encode an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; or that encode a NADP dependent malic enzyme.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Applicants fail to describe a representative number of polynucleotide sequences falling within the scope of the claimed genus of polynucleotides that have at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; that encode an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; or that encode a NADP dependent malic enzyme. Applicants only describe cDNA of SEQ ID NO:1 and the amino acid sequence of SEQ ID NO: 2. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides.

Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*.

Furthermore, given the lack of description of the necessary elements essential for polynucleotides that have at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; that encode an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; or that encode a NADP dependent malic enzyme, it remains unclear what features identify encoding polynucleotide. Since the genus of broadly claimed polynucleotides has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Sequences that have at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; that encode an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; or that encode a NADP malic enzyme encompass naturally occurring allelic variants, mutants, as well as sequences encoding proteins having no known activity, of which Applicant is not in possession.

Accordingly, the specification fails to provide an adequate written description to support the

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genus of polynucleotides encompassed by the hybridization language or percent identity language as set forth in the claims. (See Written Description guidelines published in Federal Register/Vol. 66, No.4/Friday, January 5, 2001/Notices: p.1099-1111).

Claims 1-2 and 4-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

Applicant broadly claims an isolated nucleotide sequence comprising at least 70% sequence identity to SEQ ID NO: 1; that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; a nucleotide sequence encoding an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; nucleotide sequence encoding an NADP dependent malic enzyme: Applicant also claims expression cassettes, plants and seeds comprising said nucleotide sequence, and methods of increasing protein or oil production in a plant transformed therewith.

Applicant teaches methods of transforming maize, soybean and sunflower with any pyruvate kinase or malic enzyme (specification, pages 39-48).

Applicant does not teach plants transformed with an isolated nucleotide sequence comprising at least 70% sequence identity to SEQ ID NO: 1; or a nucleotide sequence that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1; or a nucleotide sequence encoding an amino acid sequence comprising at least 75% sequence identity to SEQ ID NO: 2; or a nucleotide sequence encoding an NADP dependent malic enzyme; or plants having an increase or a decrease in expression of enzymes encoded by said polynucleotides; or methods of increasing protein or oil production in a plant transformed therewith or plants thereof; or what levels of malic enzyme expression or pyruvate kinase expression are required before increases in either protein or oil in a transformed plant will occur.

The isolation of orthologous DNA sequences from other species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited sequence identity. Thus the screen for orthologous sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous sequence encoding the same protein activity is illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun P. *et al.* Science Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

Engineering increases in either protein or oil in any plant or plant seed by any transgenic methods is highly unpredictable because there are so many variations in the amount and variety of lipid or protein end products between and even within species and there is limited knowledge of their metabolic regulation. Attempts to increase protein or oil have resulted in seeds that produce either almost entirely oil and no protein or seeds that produce mostly starch and hardly any protein or oil (Ohlrogge J. *et al.* Biochemical Society Transactions, 2000; Vol. 28, part 6, pages 567-573; see Abstract, page 568 column 1; page 570, column 1 beginning with What controls seed oil content? to column 1 page 571; and page 573, column 2).

Based upon Applicant's limited guidance one cannot predict which embodiments would be operable and thus undue trial and error experimentation would be required by one skilled in the art to isolate and synthesize the multitude of non-exemplified DNA sequences encompassed by the claims, produce expression constructs therewith, transform plants of any and all plant species, and screen through the transformed plants to identify those with increased oil or protein, if such plants are possible.

Further, the specification is not enabling for the use of SEQ ID NO: 1 because Applicant has not taught how to use SEQ ID NO: 1 in any plant for increasing either protein or oil in a transformed plant or transformed plant part.

Given the unpredictability in the art as to which plant metabolic pathway in which plant part would allow for increases in oil or protein content when transformed with either a pyruvate kinase, or NADP dependent malic enzyme or a sequence having 70% sequence identity to SEQ ID NO: 1, or a sequence that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency; the breadth of the claims encompassing any plant transformed with any

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polynucleotide having 70% sequence identity to SEQ ID NO: 1, or that hybridizes to SEQ ID NO: 1 under conditions of unspecified stringency; the lack of guidance in the examples of the specification or in the prior art as to which nucleotide sequences would increase protein or oil content in a transformed plant or what changes in the levels of endogenous expression of a malic enzyme or pyruvate kinase would result in increases in protein or oil in a transformed plant; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 and 4-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 12 and 16 recite "stringent conditions" which is a relative term comprising either low, high, or moderately stringent conditions.

Claim 16, the claim refers to specific nucleotide sequences using GenBank accession numbers that are known to change over time.

Claims 18-20 are improperly dependent. Claim 16 is a method claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-6 and 9-20 are rejected under 35 U.S.C. 102(b) as being anticipated by

Murase M. *et al.* (U.S. Patent 5,914,449 issued June 22, 1999).

Applicant broadly claims a nucleotide sequence that hybridizes under stringent conditions to SEQ ID NO: 1 operably linked to a tissue specific plant promoter, a plant transformed therewith and a method for increasing oil content in plant and plant seeds thereof. However, "stringent conditions" is indefinite as set forth supra. Applicant has not clearly defined the phrase in the instant specification, and hence the claims interpreted broadly to encompass essentially any nucleotide sequence because any nucleic acid would hybridize to SEQ ID NO: 1 under some hybridization conditions.

Murase teaches an isolated nucleic acid encoding pyruvate kinase from *B. napus* operably linked to a seed specific promoter (columns 11 and 14); a transformed *B. napus* and transformed seeds (column 14); and increased oil in transformed seeds (column 16); and teaches the method steps of introducing into a plant a nucleotide construct comprising a nucleotide sequence operably linked to a promoter that drives expression in a plant cell, and thus inherently teaches the method of increasing protein in a plant and the seed or fruit, and embryo and endosperm thereof. Thus the reference teaches all the limitations of Claims 1-2, 4-6 and 9-20.

Claims 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Jofuku K. *et al.* (U.S. Patent 5,994,622 filed August 0, 1996).

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Applicant broadly claims a method of increasing protein in any plant by transformation with any nucleotide sequence that hybridizes to SEQ ID NO: 1 under stringent conditions. However, "stringent conditions" is indefinite as set forth supra. Applicant has not clearly defined the phrase in the instant specification, and hence the claims interpreted broadly to encompass essentially any nucleotide sequence because any nucleic acid would hybridize to SEQ ID NO: 1 under some hybridization conditions.

Jofuku teaches increased protein in the seeds of *Arabidopsis* transformed with an AP2 gene from *Arabidopsis*. Thus, the reference teaches all the limitations of Claims 12-15 (columns 15 and 18, Table III). Thus, the reference teaches all the limitations of Claims 12-15.

Claims 16-20 is rejected under 35 U.S.C. 102(e) as being anticipated by Tarczynski M. *et al.* U.S. Patent 6,653,535 B1 filed May 28, 1999.

The applied reference has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant broadly claims a method for increasing a desired product in a plant or plant part by transformation with a nucleotide sequence encoding a NADP-dependent malic enzyme selected from the group consisting of GenBank Accession nos. J05130, AB016804, AW217913 and A1727829. The claim is indefinite as discussed supra. The GenBank DNA sequences

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incorporated through reference are not clearly defined in the specification, and hence the claims are interpreted broadly to encompass any other published GenBank variants of said sequences.

Tarczyński *et al.* teaches transformation of maize using NADP dependent malic enzyme J05130 (examples in columns 7 and 8) and inherently teaches a method for increasing a desired product by teaching increased productivity under conditions when water is not limiting that encompass seeds, fruits, and seed parts such as the embryo and endosperm (column 1, lines 59-61). Thus the reference teaches all the limitations of Claims 16-20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-2 and 4-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murase M. *et al.* U.S. Patent 5,914,449 in view of Applicant's admission.

Applicant broadly claims a nucleotide sequence that hybridizes under conditions of unspecified stringency to SEQ ID NO: 1 operably linked to a tissue specific plant promoter, a plant transformed therewith and a method for increasing oil content in plant and plant seeds thereof.

The teachings of Murase are discussed supra. Murase further teaches a maize seed specific zein promoter (in column 6, lines 6-7).

Murase does not teach transformation of monocots such as maize.

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Applicant admits that methods of maize transformation well known in the art, and Applicant cites the prior art patent WO 98/32326 (specification p. 41, lines 19-22).

It would have been *prima facie* obvious at the time of Applicant's invention to modify the invention of Murase to include a method for the transformation of monocots such as maize, well known in the art, to transform maize plants instead of *Brassica* plants and to include the zein specific promoter taught by Murase to increase the oil content in maize seeds. One of skill in the art would have been motivated by the success of Murase in increasing oil content in *Brassica* seeds and the teachings of WO 98/32326 of maize transformation to increase oil content in maize seeds, and that one would have had a reasonable expectation of success of expressing genes in transformed maize plants and seeds.

All claims are rejected

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
February 18, 2004

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized, flowing script.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600